

Criteria for Use of Memantine (Namenda®)

VHA Pharmacy Benefits Management Strategic Healthcare Group, Alzheimer's Disease Workgroup and the Medical Advisory Panel

The following recommendations are based on current medical evidence and expert opinion from clinicians. The content of the document is dynamic and will be revised as new clinical data becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The clinician should utilize this guidance and interpret it in the clinical context of the individual patient situation.

Introduction

Dementia is a significant cause of morbidity in the elderly population. Memantine, an NMDA receptor antagonist, has been approved for use in moderate to severe Alzheimer's disease (AD). In ambulatory, community-dwelling patients with moderate to severe AD, memantine demonstrated less functional and cognitive deterioration in comparison to placebo as measured by various rating scales. However, this difference was not apparent in the clinical impression of these changes. The data to date are from relatively short trials, 12-28 weeks in duration. Given the chronic and progressive nature of the disease, longer trials are needed to define the outcomes and benefits of this agent.

Therefore, based on the limited evidence for benefit and populations studied the criteria below provide guidance on prudent use of this agent:

Patient Selection

- Patients should have documented in their medical record a diagnosis of AD according to the criteria of the Diagnostic and Statistical Manual – IV (American Psychiatric Association, 1994). In addition, the patient should have been evaluated by a neurologist, geriatrician, geriatric psychiatrist or provider experienced in the diagnosis of AD as part of the work-up.
AND
- Have moderate to severe AD as defined by a Mini-Mental State Exam (MMSE) of less than 15
AND
- Be able to perform with minor assistance at least one self-care ADL, as defined by toileting, feeding, grooming, ambulation, bathing or dressing.
- Nursing home residents whose admission was due to the progression of their dementia, defined as not being able to perform at least one self care ADL, are not candidates for memantine therapy. Therapy should be tapered and discontinued if currently receiving memantine. Therapy naive patients fitting this description should not have therapy instituted.
- Patients should be considered for memantine monotherapy if they are treatment naïve
- If combination therapy with a cholinesterase inhibitor (CI) is considered (patients with moderate to severe dementia and MMSE<15), the patient should be community dwelling, on a stable dose of CI for 6 months and demonstrate decline or loss of stabilization in clinical status as shown by self-care ADL or other rating tools.

Dosing

- Therapy should be initiated at 5mg daily for one week, then 5 mg twice daily for one week, then 5 mg in the morning and 10 mg in the evening for one week followed by 10 mg twice daily as maintenance therapy.
- Memantine should not be used in patients receiving dialysis. In patients with a creatinine clearance of <50 ml/min a dosage adjustment to 10 mg/day is recommended. At the present time, the clinical signs of memantine accumulation are unknown.

Discontinuation

Memantine therapy should be discontinued in patients who show no clinical benefit in 6 months, when a patient becomes dependent in all self-care ADL or becomes institutionalized due to the severity of their dementia.

Precautions

Memantine is a weak base that is largely renally excreted. Alteration of urine pH to an alkaline state may lead to significant retention of the parent compound. Agents that utilize the same cationic transport mechanism in the renal tubule as amantadine may also inhibit memantine secretion. Possible agents implicated in this mechanism include cimetidine, ranitidine, hydrochlorothiazide, quinidine and triamterene. Careful monitoring should be employed if these agents are used concurrently.

Concomitant use of amantadine, ketamine and dextromethorphan should be avoided due to a theoretical additive effect at NMDA receptors.

References

1. Kornhuber J, Wiltfang J. The role of glutamate in dementia. J Neural Trans 1998;(suppl 53):277-287.
2. Product labeling, Namenda®(memantine); 2003: Forest Pharmaceuticals. St. Louis, MO.
3. Parsons CG, Danysz W, Quack G. Memantine is a clinically well tolerated N-methyl-D-aspartate (NMDA) receptor antagonist: a review of preclinical data. Neuropharmacology 1999;38:735-767.
4. Jarvis B, Figgitt DP. Memantine. Drugs Aging 2003;20(6):465-476.
5. Guay DRP. Drug Forecast: Memantine, prototype of a new approach to treatment of dementia. Consultant Pharmacist 2003;18(7):625-634.
6. Areosa Sastre A, Sherriff F. Memantine for dementia. Cochrane Database of Systematic Reviews 2003;3: CD003154.
7. Tariot P, Farlow MR, Grossberg GT, et al. Memantine/treatment in patients with moderate to severe Alzheimer Disease already receiving donepezil. A randomized controlled trial. JAMA 2004;291:317-324.
8. Reisberg B, Doody R, Stöffler A, et al. A randomized, placebo controlled study of memantine, an uncompetitive NMDA antagonist, in patients with moderate to severe Alzheimer's disease. N Engl J Med 2003;348:1333-1341.
9. Orgogozo JM, Rigaud AS, Stöffler A, et al. Efficacy and safety of memantine in patients with mild to moderate vascular dementia, placebo controlled trial (MMM 300). Stroke 2002;33(7):1834-1839.
10. Wilcock G, Möbius HJ, Stöffler A. A double blind placebo controlled multicentre study of memantine in mild to moderate vascular dementia (MMM 500). Int Clin Psychopharmacol 2002;17(6):297-305.
11. Winblad B, Poritis N. Memantine in severe dementia; results of the 9M-Best study (benefit and efficacy in severely demented patients during treatment with memantine). Int J Geriatr Psychiatry 1999;14(2):135-146.

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Contact person: Kathryn Tortorice, Pharm D, BCPS
Clinical Specialist
Department of Veterans Affairs
Pharmacy Benefits Management Strategic Health Group (119D)
Hines VA Hospital
1st Avenue- 1 Block North of Cermak Rd
Building 37, Room 139
Hines, IL 60141